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Patentanmeldung Nr. Patent application No. Demande de brevet n°

02077434.5

PRIORITY DOCUMENT
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For the President of the European Patent Office

Le Président de l'Office européen des brevets
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Nutritional or pharmaceutical compositions for increasing the methylation reaction capacity of organisms

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NUTRITIONAL OR PHARMACEUTICAL COMPOSITIONS FOR INCREASING THE METHYLATION REACTION CAPACITY OF ORGANISMS.

FIELD OF THE INVENTION

The present invention relates to a nutritional or pharmaceutical composition comprising a L-serine containing-component and an energy metabolism precursor wherein the composition is substantially free of glycine. A process for making such composition is herein provided as well as the use of the L-serine containing-component for increasing the methylation reaction capacity of organisms, preferably the creatine response within mammals muscle.

BACKGROUND OF THE INVENTION

Adenosine triphosphate (ATP) is the immediate source of energy for allowing many processes in the mammals body such as biosynthetic and metabolic pathways, for maintaining ionic gradients and transport over membranes and for muscle contraction. ATP is metabolised in the muscle by the cleaving of one phosphoryl group. The chemical energy produced from this group can then be used to contract the muscle. As a result, adenosine diphosphate (ADP) *is* produced as a by-product. ATP can be produced in the muscle from glycogen or phosphocreatin. Phosphocreatine provides a ready source of energy-rich phosphoryl groups and is able to resynthetise ATP at nearly twice the rate compared to glycogen.

However, the amount of ATP in the muscle is small. Therefore a reserve supply of readily available energy is needed.

Phosphocreatine in muscle cells serves as a reservoir of high potential phosphoryl group. Creatine enters the muscle tissue by active transport where it can be converted to

phospho-creatine by the action of mitochondrial or cytosolic kinases. The reversible transfer of a phosphoryl group from creatine phosphate to ADP to form ATP keeps the intracellular ratio of the amounts of ATP to ADP high. Muscle fatigue and the accumulation of lactic acid occur in energy-deficient states.

Creatine is a nitrogenous acid distributed in the mammals body in many tissues, e.g. in muscular tissue, but also in liver, pancreas, brain, retina, testes and kidneys . It has the chemical name N-methyl-N-guanylglycine. Creatine is synthesised in the body through the processing of the amino acids glycine, arginine, and methionine and is supplied to the body by the food intake.

Creatine is available from many food sources and can be found in the muscle of most mammals and fish, including beef, chicken, cod, herring, pork, salmon, tuna and turkey. However, a problem encountered with the supplying of creatine via cooked food is that the cooking process tends to deteriorate the creatine. Further, most of the high creatine-containing food are also high in fat and cholesterol, thus minimising the interest for high intake of creatine via food.

Still, the supply of creatine to the body to enhance physical performance has become a popular habit as a substitute for steroids and other drugs in various sport and body building regimes. Indeed, because creatine is an amino acid normally biosynthesised in vertebrates, it is not included in the list of components that are prohibited for use as published by the International Olympic Committee, which list includes more than 120 kinds of products.

Accordingly, creatine supplements have become a popular source of obtaining the nutrient, especially for the body-building industry, e.g to increase lean body mass and among athletes e.g to increase working capacity.

Another category of persons to which the supply of creatine supplements is beneficial are those persons where a high demand is put on the body to provide sufficient energy, i.e. ATP. These include, but are not limited to, persons where the blood supply has

been imparted such as after a trauma, disease affected persons, or even vegetarians people.

The use of creatine in the production of supplements is widely known, especially in the area of sport.

Hence, US 5,973,005 discloses a drink comprising an aqueous solution of creatine, wherein the creatine is under the form of creatine acid sulfate, for providing a source of creatine to an animal in need thereof.

US 6,136,339 discloses the combination of creatine with lipoic acid for enhancing an athlete muscle's size or strength.

US 6,172,114 discloses the combination of creatine with ribose for increasing muscle strength while reducing the side effect linked with creatine, namely diarrhea and nausea.

Creatine containing supplements are also discussed by Gregory S. Kelly, N.D in Alt. Med Rev. 1997; 2(3):184-201. In this article, a suplement routine comprising creatine monohydrate, protein shake, vitamin C, and a multivitamin/mineral formulation is described as providing best result on the athletes strength.

However, a problem associated with the use of creatine is that in order to provide a significative response of creatine within the mammals muscle, a relatively large dose of creatine (2 to 20g per day) has to be administered to the mammals. This high dosage can impart the normal dietetic patterns and induces diarrhee or even nausee. Further, it was also reported in Stead L.M. et al, Am J Physiol, 281, E1095, 2001, that consumption of large amounts of creatine by rats, taking a dosage that is equivalent to a dose of 20g creatine for a subject of 70kg per day, i.e. 0.28g of creatine per kilo and per day, could lead to a decrease in the capacity of endogenous creatine biosynthesis due to a decrease in the expression of L-arginin:glycine amidinotransferase. However, decreasing the capacity of endogenous creatine biosynthesis is undesirable, especially when specific high demands on methylation capacity are required like during diseases

or surgery. Accordingly, one solution known in the art to remediate to this decrease is to discontinue the usage of creatine for a certain period on a periodic basis.

In addition, creatine is unstable in aqueous solution, and tends to form creatinine when present in acidic conditions. Creatinine is the inactive form of creatine and is quickly excreted from the body. Creatinine cannot be converted into phosphocreatine and does not participate in the regeneration of ATP. Consumption of creatinine may complicate the interpretation of the increase of creatinine levels due to disease such as kidney disorders.

Further, creatine appears to increase water retention and water content of tissue, which may disturb electrolyte balance. A case of glomerulosclerosis was recently reported.

Accordingly, there is a need for a composition that provides an effective creatine response in the mammals muscle without causing the side effects linked to the use of creatine or having the safety problems linked with the use of creatine.

One solution to this problem is to use an energy metabolism precursor of guanidino-acetic acid (GA) type or also called glycocyamine or N-amidinoglycine in the literature.

In mammals, GA is a natural precursor of creatine and is produced from arginine which transfer its amidino group to the glycine, thereby resulting in the formation of GA. GA can then be converted into creatine by methylation with a methyl transferase present in many tissues of the mammals, which uses S-adenosyl methionine (SAM) as a substrate.

Use of GA in therapeutic composition is known from US 2,761,807 but is also known from commercially available sport nutrition supplements.

US 2,761,807 discloses the combination of GA with a material selected from betaine, betaine hydrate, choline, and dimethylthetin for providing a source of energy in the treatment of cardiovascular diseases, paresis resulting from poliomyelitis, multiple scleropsis, and the anxiety-tension-fatigue syndrome. The described amount of GA to

be administered is of 30 mg GA per pound body weight per day, which results in the consumption of about 4.6-6g GA per day, dependent on the body weight. The material selected from betaine, betaine hydrate, choline, and dimethylthetin are to be included in a 3-5 fold molar excess compared to GA, thus, taking betaine as example in 4 fold molar excess, resulting in the consumption of 20g of betaine. This results in the consumption of a high amount of a composition of about 25g of powder per day, which appears burdensome in a conventional dietetic pattern especially when the taste of the active components itself is not to be appreciated. This problem of undesirable taste is even more acute among athletes, who are regular users of such compositions. One solution to minimise the undesired taste is by mixing with other ingredients or by dissolution in liquid at for example a 5% dissolution rate. However, dissolution would then require them to drink a volume of at least 500ml per day.

Sport nutrition supplements are also available on the market. For example, Syntrax Innovations markets Swole as a product for non-creatine responders. This product contains per serving of 7g: 1.5g GA, 2.5g glucuronolactone, 2g creatine and 0.5 dimethylglycine. Two serving per day are recommended. This results in the consumption of 14g dry powder of the supplement composition, which in turns requires drinking 250 ml of diluted supplement composition.. Further, the supplement uses glucoronolactone, which is in itself an expensive component, thereby increasing the cost of the resulting composition. Again, this supplement also comprises unpallatable components, i.e. components with an undesired taste.

It has been found that reduction of the amount of unpalatable components within supplement compositions should preferably be lower than 10g, and preferably below 6g on a daily basis to provide a more desirable taste.

Further, GA has also been reported as being epileptogenic, especially with patients with inherited decrease of the GAMT expression. GA has also been associated with undesired side effects due to the accumulation of GA, thus causing a distortion in the creatine, methylation and energy metabolism.

Still, persons suffering from a metabolic stress such as the ones which occur after surgery, traumata, malnutrition or in catabolic states encounter a problem with the capacity of methylation reaction of their organism. Rapidly proliferating or differentiating tissues such as epithelial cells, e.g. of the gastrointestinal tract, bone marrow, endo- or exocrine tissues such as some tissues in the gonades are particularly sensitive to metabolic stress, thus hindering or reducing the capacity of the organism of methylation reactions.

Insufficient methylation capacity can be detected by measuring the capacity of a tissue to generate SAM per time unit. As an indicator of methylation capacity is the presence of a high level of homocystein in the blood plasma after an overnight fasting. It has been found that large groups of persons suffer in their daily life from such elevated homocystein levels. High levels of homocystein in the blood plasma can also arise from disorders in the organs or from diseases states.

Nevertheless, in mammals, methylation of components is an important process reaction. Indeed, as described hereinbefore, GA is converted into creatine by a methylation reaction.

Accordingly, there is a need for a composition that is effective in decreasing homocystein levels, shows no or reduced occurrences of side effects due to the use of the composition while still maintaining the methylation capacity.

It is also an object of the invention to produce a composition that has one or more of the following object: good taste, reduced cost, and/or that do not require, if the composition used as a supplement is diluted, to drink a high amount of the diluted composition, i.e. preferably no more than 150 ml, most preferably no more than 100 ml.

It has now advantageously been found that the use of a protein component that comprises a high level of serine contained therein fulfils such a need and further acts as effective aid for the metabolism of energy.

It has further been found that the combination of such protein containing L-serine with an energy metabolism precursor of the GA type was also effective in producing an effective creatine response to the mammals muscle without producing the side effect of creatine.

Not to be bound by theory, it is believed that L-serine induces the methylation of GA or equivalents thereof via a series of reaction ending in the methylation of GA into creatine.

The use of L-serine, in particular in high amount, is not recognised in the art. To the contrary, in mammals, serine is considered as a non essential amino-acid for nutrition or pharmaceutical compositions. Hence, Gregory S. Kelly, N.D in Alt. Med Rev. 1997; 2(3):184-201 prescribed the use of protein, in particular whey protein to provide the sufficient levels of amino acid, mainly sulfur amino acid (methionine and cysteine), branched amino acid (leucine, isoleucine and valine) but also glutamine and glycine. Proteins always contain serine and glycine. The table below gives the weight ratio associated with various type of proteins:

Type of protein	Weight ratio of serine: Glycine
Whey proteins isolated from bovine milk	about 2.5
soy protein	about 1.2
organ meat	<1
total chicken egg	2.2
chicken egg yolk	2.6
vegetable protein	<1.5

Thus, it can be said that serine is not considered to be an important dietetic amino acid. Instead, it is either considered to be sufficiently quantitatively present in the dietetic protein, i.e. provided by food intake, or that the presence of glycine and alanine that are present in the dietetic protein can ensure sufficient serine biosynthesis to produce high levels of serine. However, it has now been found that the presence of a high level of glycine hinders the action of the serine. It is speculated that glycine which acts a methyl acceptor will interact with serine which acts a methyl donor.

SUMMARY OF THE INVENTION

There is a provided a nutritional or pharmaceutical composition comprising:

a)-a protein containing L-serine; and

b)-an energy metabolism precursor selected from glycocyamine (GA), equivalents thereof, and mixtures thereof, and

wherein the composition is free of glycine or if glycine is present within the composition, the weight ratio of L-serine: glycine after hydrolysis of the composition is of at least 2.7:1.

In another aspect of the invention, there is provided a process for making said composition.

In a further aspect of the invention, there is provided the use of the composition for increasing the capacity of methylation reaction of the organism, thereby increasing the creatine response within mammals muscle.

Still, in another aspect of the invention is provided the use of the protein containing L-serine for the preparation of nutrition or pharmaceutical composition for increasing the methylation capacity of the organism, thereby increasing the creatine response, wherein the protein containing L-serine comprises no glycine or if present the weight ratio of L-serine: glycine after hydrolysis of the protein containing L-serine is of at least 2.7:1.

It is also believed that the presence of the protein containing L-serine is beneficial to the effect linked to the energy metabolism precursor of the GA type on the enzyme described in Am. J. Physiol. Endocrinol. Metab., Nov. 2001, 281 (5): E1095-E1100, and thus beneficial to health. Indeed, the increase in methionine synthase increases in turn the methylation capacity of the organism but only on the condition that sufficient substrate is present. It has been found that a substrate containing a high level of serine, with preferably sufficient levels of cofactors like vitamin B6, folic acid, vitamin B12 and zinc is an effective substrate.

Further, it is also believed that by the present invention, an increase in cysthathione synthase is obtained, which provides an increase in the endogenous cysteine production, and in turn provides under certain conditions an increase in the glutathion biosynthesis and sulphation capacity.

DESCRIPTION OF THE INVENTION

Protein containing L-serine

A protein containing L-serine is an essential component of the invention. For the purpose of the invention, a protein containing L-serine has been found advantageous for increasing the methylation capacity of the organism, thereby increasing the creatine response. However, to provide this effect, the protein containing L-serine, in particular when incorporated in nutrition or pharmaceutical composition, needs to be present within the composition either in the absence of glycine or if glycine is present within the L-serine containing-component and/or final composition, it is then required that the weight ratio of L-serine: glycine after hydrolysis of the final product is of at least 2.7.

L-serine, also called serine herein, can endogeneously be formed by transamination of hydroxypyruvate but can also be formed from glycine, e.g. the glycine that is formed from choline degradation, via betaine, dimethylglycine and sarcosine. L-serine is also present in proteins. Functional equivalents can also be used herein in addition or in place of the L-serine.

By "protein containing L-serine" it is meant protein containing L-serine but also L-serine containing component selected from L-serine, equivalents thereof and mixtures thereof. By "equivalents", it is meant L-serine in its zwitterion form, L-serine in its salt form, optionally coupled to the amino or carboxy group, peptides, proteins, and mixtures thereof". For the purpose of clarity, phosphatidylserine is not considered as a suitable "equivalent".

The requirements for the peptides and protein to be used as L-serine containing components are that:

1)-they can be digested in the total gastrointestinal tract to form serine or can provide serine after metabolism of the peptides in the liver, and

2)-they provide a weight ratio of L-serine to glycine after hydrolysis of the final product of at least 2.7:1

As described herein before, it is essential for an effective methylation capacity that the weight ratio of L-serine to glycine within the protein component, if used alone, or if incorporated in the composition comprising the energy metabolism precursor is of at least 2.7:1; preferably of at least 2.9:1; more preferably of least 3.1:1; and most preferably of at least 3.4:1. It is also preferred that the total doses of serine is not too high because this may impart normal dietetic practices. In a supplement the weight ratio of Serine to glycine can be relatively high because serine can be the only amino acid that is included in the preparation. However in a complete composition also glycine will be present which causes the ratio to be typically below 6:1 and preferably below 4:1.

Food grade qualities of L-serine are commercially available from Degussa and other amino acid manufacturers. Proteins such as caseinates from milk or egg proteins are also readily available.

Levels within the composition will depend on type of product. Nutritional supplements will typically comprise 25-90% protein component.

Dosage:

When the L-serine containing component is used in a nutritional supplement, a dose of at least 1g per day should be administered so that at least 0.75g excess L-serine is consumed compared to glycine, preferably a dose of at least 1.2g L-serine so that at least 1g excess L-serine is consumed compared to glycine, and more preferably a dose of at least 1.8g L-serine so that at least 1.5g excess L-serine is consumed compared to glycine. Preferably, the daily dosage amounts to up to 30 g, more preferably up to 15 g.

When the L-serine containing component is used in a complete nutrition composition, a higher dose of L-serine will be used, i.e. of at least 4.8g per day should be administered

so that at least 3.2g excess L-serine is consumed compared to glycine, preferably a dose of at least 5.5g L-serine so that at least 3.9g excess L-serine is consumed compared to glycine, and more preferably a dose of at least 6.4g L-serine so that at least 4.7g excess L-serine is consumed compared to glycine. Preferably, the daily dosage amounts to up to 30g, more preferably up to 20 g.

By "glycine", it is meant the amino acid per se. Sarcosine or dimethylglycine are not included by the term "glycine". Accordingly, when the weight ratio of serine to glycine have to be determined for a specific peptide, protein, or mixture of amino acids with proteins or peptides, the hydrolysis of the final product or mixture will have to be performed. A suitable method of determination of the L-serine:glycine weight ratio for use herein is given in The AOAC Official methods of Analysis 1984, nr 43.263 and 43.264.

Still another suitable method of determination of the L-serine:glycine weight ratio for use herein is by calculation from published standard values.

It is further preferred to include a relatively low level of guanidino compounds other than GA or equivalent thereof and Creatine in the nutritional compositions. These compounds are arginine, ornithine or citrulline or their functional equivalents such as salts. These compounds impart a further creatine response of the GA and Creatine in the product. Typically serine levels in the protein component, when these component are present are then more than 1.7 times and preferably above 1.8 and most preferably above 2.2 that of the levels of arginine, citrulline or ornitine.

The amount of GA or equivalent thereof should therefore be at least 0.3 times the total amount of other guanidino compounds and preferably at least 0.5 times the amount of arginine, citrulline or ornitine.

It is further preferred to include a minimum amount of L-methionine in the composition of at least 0.5 g per daily dose, and preferably more than 0.8 g. L-methionine can be present as pure amino acid, its salt or as peptide or protein.

It is also preferred to include L-histidine in an amount of at least 0.5 and preferably more than 0.8 g per daily dosis. L-His can be present as pure amino acid, as salt, peptide or protein.

Energy metabolism precursor

The energy metabolism precursor for the purpose of the invention is selected from guanidino-acetic acid (GA), equivalents thereof, and mixtures thereof. GA is a natural energy metabolism precursor of creatine: GA results from the transfer of the arginine's amidino group to glycine, which in turn gives GA.

For the purpose of the invention, GA or equivalent thereof are used as energy metabolism precursors. Accordingly, GA can be used in its pure acid form.

By "equivalents thereof", it is meant:

-compounds which would provide GA in blood plasma after oral consumption and which are preferably selected from guanidino-acetic acid salts of sodium, potassium, calcium, ammonium, magnesium, zinc, iron, copper, chromium and mixtures thereof,

-ester and/or ether compounds that can be metabolised to guanidino-acetate in the gut or body, e.g. by hydrolysis, i.e. preferably esters of the carboxy group with lower organic acids and selected from esters of acetic acids, esters of propionic acid, esters of butyric acid, and mixtures thereof. Advantageously, these esters are stable in solution, thus making them suitable for incorporation into liquids, in particular drinks or for enteral administration.

Further suitable compounds as "equivalents" are compounds where the amidino group of the GA is modified by protonation and thus forms a salt with, for example, anions that are commonly used in food manufacture, such as chloride, bicarbonate, and hydroxide. For the purpose of the invention, it is preferred not to use anions that might promote nitrite formation in vivo, such as nitrate, nitrite, or sulphite.

Dosage:

For the purpose of the invention, the amount of energy metabolism precursor to be employed in the invention of the composition is linked to the excess of L-serine versus glycine. Accordingly, on a molar basis, it is preferred that the molar amount of energy metabolism precursor to be daily administered lies within the range of from 0.1-10 times the excess of L-serine versus glycine, and more preferably lies within the range of from 0.2-4 times the excess of L-serine versus glycine.

Stated otherwise in terms of daily dosage per se of energy metabolism precursor, it is preferred that the energy metabolism precursor is administered to mammals at a low dosage per day of at least 0.2g, preferably at least 0.5g, more preferably at least 0.7g, and up to 4g, preferably up to 3g. In particular, during chronic use, a low daily dosage of energy metabolism precursor between 0.8-3g was found effective to produce an effective and safe creatine response from the energy metabolism precursor.

Optionals

The composition of the invention may also comprise optionals which will further secure an adequate methylation capacity of the organism. Preferred optionals for use herein are selected from creatine, vitamins, carbohydrates, aldehydes, mineral, and mixtures thereof.

Creatine

Addition of creatine to the invention composition has been found advantageous. Indeed, it has been found that by addition of creatine to the invention composition, the creatine response was increased without causing the known side effects of creatine. Further, it has also been found that by addition of a low amount of creatine, the amount of energy metabolism precursor could even be decreased. Accordingly, a much lower daily dosage of energy metabolism precursor could be used whilst still providing an effective and safe creatine response.

Not to be bound by theory, it is believed that due to the synergy between the activity of creatine and the energy metabolism precursor, lower doses can be used so that the expression of the rate limiting enzym arginin:glycine amidinotransferase decreases to a

much lower degree than by using high doses of creatine alone, thereby decreasing to a much lower extent the capacity of endogenous creatine biosynthesis.

Thus, in the presence of creatine, a daily dosage of energy metabolism precursor within the range of from 0.1g to 3g, preferably of from 0.4g to 3g, more preferably 0.5-2.4g of GA was found effective. The creatine, when present, is present in weight ratio of energy metabolism precursor:creatine of from 0.2:5, preferably from 0.6:4.5, more preferably from 1.1:4, and most preferably from 1.2:3.6.

Creatine, when present, can be used as it is and/or in its salts form and/or in its hydrate form. Suitable salts of creatine for use herein are those selected from salts of creatine with inorganic acid (preferably creatine phosphate, and/or creatine chloride), salts of creatine with organic acid (preferably creatine citrate and/or creatine pyruvate and/or creatine malate and/or creatine fumarate and/or creatine isocitrate). For the purpose of the invention, it is preferred to use salts of creatine with organic acid.

Vitamins

Vitamins are also preferred optional for the purpose of the present invention. Indeed, it has been found that addition of vitamin, in particular those selected from vitamin B6, vitamin B12, folic acid, and mixtures thereof, produces a further increase in the creatine response.

Carbohydrate

The composition of the invention can optionally comprises a carbohydrate. A suitable carbohydrate for use herein is maltodextrin.

Minerals

Minerals can also be advantageously used in the invention composition. Suitable minerals for use herein are selected from chromium, vanadium, selenium, magnesium, boron, zinc, and mixtures thereof, preferably magnesium and/or zinc.

The composition of the invention may further optionally comprises minors such as natural and/or artificial flavoring components, dyes or other coloring additives, preservatives, lubricants, binders, and fillers.

Form of the composition

The composition of the invention may be in any form suitable for its administration whether orally or enteral administration. Typical forms suitable for use herein include liquid form, powder form, emulsion form, suspension form, gel form, bar form, but also cookies or sweeties.

Use/applications

There is provided the use of a composition of the invention for increasing the methylation reaction capacity within mammals organisms, which in turns increases the creatine response within mammals muscle.

Also provided herein the use of a protein containing L-serine for the preparation of a nutritional or pharmaceutical composition for increasing the methylation reaction capacity of organisms, preferably the creatine response within mammals muscle, and wherein the protein containing L-serine comprises no glycine or if present the weight-ratio of L-serine: glycine after hydrolysis of the L-serine containing component is of at least 2.7:1.

Administration of the invention composition or protein containing L-serine according to the invention has been found beneficial to diseases affected persons, such as hospitalised persons, persons suffering from mild health problems or who want to prevent a further worsening of their condition, in particular when suffering from cardiovascular, cerebrovascular, ischaemic diseases or disorders associated with problems with creatine metabolism or energy supply but also vegetarian persons, elderly persons, infants, in particular those having small birth weight and thus having an anabolic reaction, athletes including also persons that require an increase in lean body mass.

The following is a list with abbreviations that are used in the examples:

Abbreviations	Definition
GA	Guanidino-acetic acid
Creatine Pyruvate	Creatine Pyruvate
vitamin premix 1	vitamin premix on maltodextrin basis providing 200μg folic acid, 2μg cyanocobalamine and 2mg vitamin pyridoxine
Milk protein	Milk protein providing about 0.48g L-serine and 0.16g glycine
vitamin premix 2	vitamin premix providing 400μg folic acid monoglutamate, 1μg cyanocobalamine and 3mg vitamin pyridoxine
Carbohydrate 3	maltodextrin
Lipids	Mixtures of vegetable oils or marine oils as
Vitamin premix 3	vitamin premix providing 30μg folic acid, 0.2mg Vitamin B6 and 0.3μg vitamin B12

The following are non-limiting examples illustrating the invention.

Example 1

Powder packed in sachet of 5g and comprising:

Component	Levels
GA	1.5g
Creatine pyruvate	0.5g
L-serine	2g
Vitamin premix 1	1g

The powder contained in the sachet is meant to be dissolved in a suitable liquid such as water, juice, milk, pudding, or sauce for convenient administration.

Example 2

Bar comprising per 25g:

Component	Levels
Carbohydrate	12g
Milk protein	8g
L-serine	0.6g
Tricreatine	0.5g
GA	0.5g
Vitamin premix 2	1g
Moisture	up to 25g

Example 3

Complete nutrition composition in powder form for an hospitalised patient:

Component	Levels
Caseinate	4.0g
L-serine	0.1g
GA	0.1g
Creatine pyruvate	0.1g
carbohydrate 3	12.3
Lipids	3.9g
Vitamin premix 3	1g
Moisture	up to 25g

The powder contained in the sachet is meant to be dissolved in a suitable liquid such as water prior to use, such as by tube feeding, to provide 1 kcal per ml, i.e dissolved in water and will normally be administered so that an amount of 2000 kcal is consumed.

CLAIMS

1-A nutritional or pharmaceutical composition comprising:

a)-a protein containing L-serine; and

b)-an energy metabolism precursor selected from glycocyamine (GA), equivalents thereof, and mixtures thereof, and

wherein the composition is free of glycine or if glycine is present within the composition, the weight ratio of L-serine: glycine after hydrolysis of the composition is of at least 2.7:1.

2-A composition according to Claim 1, wherein the energy metabolism precursor is administered at a daily dosage of at least 0.2g up to 4g per day.

3-A composition according to either one of Claim 1 or 2, wherein the protein containing L-serine, present within a nutrition or pharmaceutical supplement, is administered at a daily dosage of at least 1g per day.

4-A composition according to either one of Claim 1 or 2, wherein the protein containing L-serine, present within a complete nutrition or pharmaceutical composition, is administered at a daily dosage of at least 4.8g per day.

5-A composition according to any one of Claims 1-4, wherein the energy metabolism precursor and the protein containing L-serine are present in a molar ratio of from 0.1:1 to 10:1.

6-A composition according to any one of Claims 1-5, wherein the composition further comprises creatine.

7-A composition according to Claim 6, wherein the energy metabolism precursor and creatine are present within the composition in a weight ratio of energy metabolism precursor:creatine of from 0.2:5.

8-A composition according to any one of Claims 1-7, wherein the composition further comprises vitamins, preferably selected from vitamins B6, vitamins B12, folic acid, and mixtures thereof.

9-A composition according to any one of claim 1-8, wherein the composition further comprises a carbohydrate, preferably is maltodextrin.

10- A composition according to any one of claim 1-9, wherein the composition further comprises an aldehyde.

11-A composition according to any one of claim 1-10, wherein the composition further comprises a mineral, preferably selected from magnesium, zinc, and mixtures thereof, more preferably is a mixture of magnesium and zinc.

12-A composition according to any one of Claims 1-11, wherein the composition is in a form selected from liquid form, powder form, emulsion form, suspension form, gel form, bar form, cookies, sweeties, preferably powder form.

13-Use of a composition as defined in any one of Claims 1-11 for increasing the methylation reaction capacity of organisms, preferably the creatine response within mammals muscle.

14-Use of a composition according to Claim 13, wherein said composition is administered to an athlete

15- Use of a composition according to Claim 13, wherein said composition is administered to disease affected persons or vegetarian persons, or elderly persons.

16-Use of a protein containing L-serine for the preparation of a nutritional or pharmaceutical composition for increasing the methylation reaction capacity of organisms, preferably the creatine response within mammals muscle, and wherein the protein containing L-serine comprises no glycine or if present the weight ratio of L-serine: glycine after hydrolysis of the protein containing L-serine is of at least 2.7:1.

ABSTRACT

There is provided a nutritional or pharmaceutical composition comprising a protein containing L-serine and an energy metabolism precursor wherein the composition is free of glycine or if glycine is present within the composition, the weight ratio of L-serine: glycine after hydrolysis of the composition is of at least 2.7:1, which composition provides an effective increase of the methylation reaction capacity of organisms, and preferably increases the creatine response within mammals muscle.

The use of the protein containing L-serine for increasing the methylation reaction capacity of organisms, preferably the creatine response within mammals muscle is also herein provided.